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Methicillin-resistant *Staphylococcus aureus* infection in a cardiac surgical unit

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Background: Increased antibiotic resistance of common bacteria is attributed in part to the widespread use of various antibiotic agents. Prophylactic and therapeutic antibiotic treatments are routinely used in cardiac surgical units, and it is no surprise that methicillin-resistant *Staphylococcus aureus* infection is becoming a major cause of surgical infections in cardiac patients.

Methods: We reviewed our experience with patients who underwent cardiac surgery and experienced infection caused by methicillin-resistant *Staphylococcus aureus.* Between 1992 and 2000 at the Montreal Heart Institute, 39 patients had methicillin-resistant *Staphylococcus aureus* surgical infections, and 13,199 patients underwent cardiac surgery. The yearly incidence of methicillin-resistant *Staphylococcus aureus* infection, the relative risk of acute mediastinitis and of superficial wound infections or other types of methicillin-resistant *Staphylococcus aureus* infection episodes, and the effect of preventive measures were analyzed.

Results: The annual incidence of methicillin-resistant *Staphylococcus aureus* acute mediastinitis decreased from 0.37% (5/1321) of cardiac patients in 1992 and 0.44% (6/1355) in 1993 to 0% between 1994 and 1997, 0.13% (2/1528) in 1999, and 0% (0/1700) in 2000. The total incidence of methicillin-resistant *Staphylococcus aureus* infection, including mediastinitis, superficial and deep sternal and leg wound infection, and all systemic infection episodes ranged from 0.68% of patients in 1992 and 0.96% of patients in 1993 to 0.46% of patients in 1999 and 0.53% of patients in 2000. The relative risk of severe mediastinal methicillin-resistant *Staphylococcus aureus* infection to all other methicillin-resistant *Staphylococcus aureus* infection episodes decreased from 1.65 in 1992 to 0.41 in 1999 and 0 in 2000. Beginning in 1993, all patients given a diagnosis methicillin-resistant *Staphylococcus aureus* infection and all nasal carriers of methicillin-resistant *Staphylococcus aureus* were strictly isolated on the surgical unit, and vancomycin was used as the prophylactic antibiotic agent for cardiac surgery in these patients. Moreover, since 1998, all patients admitted in the hospital were screened, and nasal carriers were isolated and treated with topical antibiotic ointment.

Conclusion: Mediastinal and other infections caused by methicillin-resistant *Staphylococcus aureus* have a significant morbidity in cardiac surgical patients. After an outbreak of methicillin-resistant *Staphylococcus aureus* mediastinal infections, several preventive measures to control methicillin-resistant *Staphylococcus aureus* contamination of surgical patients were implemented (nasal screening, preventive isolation, application of mupirocin, prophylaxis with vancomycin and alcohol gels) and were effective in decreasing the incidence of methicillin-resistant *Staphylococcus aureus* infection and mediastinitis after cardiac surgery.

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Surgical infections, either wound or systemic infections, are frequent causes of morbidity and mortality after cardiac surgery. Although the incidence of sternal wound infection remains lower than 2% to 3%, several patients have bloodstream and systemic infections during and immediately after a hospital stay for cardiac surgery.[1,2] Gordon and colleagues[2] have suggested that *Staphylococcus aureus* was the most common organism causing bloodstream infection after cardiac surgery, and Mossad and colleagues[3] identified that *Staphylococcus epidermidis* was emerging as a significant agent causing sternal wound infection. Of interest, 92% of isolated coagulase-negative staphylococci were methicillin resistant in the latter study. Whereas short-term antibiotic prophylaxis of less than 48 hours was proved effective in decreasing surgical-site infections after cardiac surgery,[4] prolonged use beyond 48 hours after the operation was not only shown ineffective in preventing surgical infection, but it was also correlated with an increased risk of acquired antibiotic resistance.[5]

In 1992, we encountered an outbreak of methicillin-resistant *Staphylococcus aureus* (MRSA) infections in our cardiac surgical unit. Preventive and therapeutic measures were adopted. The objective of the present study is to review the effect of anti-MRSA preventive measures on the incidence of MRSA infection after cardiac surgery.

Methods

Hospital Setting

The Montreal Heart Institute is a tertiary cardiac care facility of 155 beds with 24 surgical intensive care units and 29 regular surgical cardiac care beds. Seventy-five percent of our surgical patients are referred from surrounding hospitals for cardiac catheterization and cardiac surgery.

Patients who underwent cardiac surgery between 1992 and 2000 were administered preoperative and postoperative antibiotic prophylaxis with either cefazolin or vancomycin for penicillin-allergic patients. The antibiotics were administered during the first 24 hours after the operation.

Definition of the Type of Infection

Sternal wound infections were classified as superficial infections characterized by purulent drainage from the wound with cutaneous and subcutaneous involvement, deep wound infections were classified as involving deep soft fascial and muscular tissue, and acute mediastinitis was defined by a purulent drainage involving the sternal bone and surrounding mediastinal tissue.[6] All suspected surgical wounds (sternal and leg wounds), urine, bronchial secretion, and blood in febrile patients were cultured.

Active surveillance of all infections occurring in surgical patients was performed by a clinical nurse specializing in infectious epidemiology and complications. We retrospectively reviewed all patients with MRSA-positive cultures and all patients with mediastinal infections after cardiac surgery during the study period.

Preventive Measures

From 1993 to 2000, all patients given a diagnosis of MRSA infection and all nasal carriers of MRSA identified by means of preoperative screening of surgical patients were strictly isolated from all other patients in a private room on the surgical unit before and after surgical intervention. Vancomycin was used as the prophylactic antibiotic agent for cardiac surgery in these patients. Nasal carriers were treated with topical mupirocin antibiotic ointment. Since 1998, all patients admitted to our hospital have been screened, and nasal carriers are isolated and treated with topical mupirocin ointment. Alcohol gel is also used in association with hand washing re-enforcement. Urgent patients were also screened and isolated if the result showed that a patient is an MRSA carrier. The results were usually available in less than 24 hours.

Case-control Study

To analyze and compare clinical, bacteriologic, and treatment results of MRSA acute mediastinitis, we retrospectively collected clinical and bacteriologic data of all patients with a diagnosis of non-MRSA acute mediastinitis during the same time period. Fifty-one patients showed clinical evidence of acute mediastinitis and formed the control group of our case-control analysis.

Statistical Analysis

Data are expressed as means and SDs. Differences between means were analyzed with the Student *t* test, and the Fisher exact test was used for categoric variables. The annual incidence of MRSA infection, the relative risk of acute mediastinitis, and the relative risk of superficial wound or other types of MRSA infection episodes are presented with 95% confidence limits. The actuarial method was used to analyze survival in our groups of patients.

Results

Patient Population

Between 1992 and 2000, of 13,199 treated patients, 39 surgical patients had an MRSA infection episode. Thirteen patients had acute mediastinitis, 13 patients had a superficial sternal wound infection, and 6 patients had a leg wound infection after saphenous-vein harvesting. Five patients showed evidence of MRSA pneumonia, and an MRSA bloodstream infection in 2 other patients after cardiac surgery was documented. Fifty-one patients showed evidence of mediastinal infection with non-MRSA organisms during the study period.

MRSA mediastinitis occurred in 3 patients after double internal thoracic artery grafting, in 7 patients after single internal thoracic artery grafting, in 2 patients after heart transplantation, and in 1 patient after aortic valve replacement. Non-MRSA mediastinitis occurred after double internal thoracic artery grafting in 10 patients, after single internal thoracic artery grafting in 24 patients, after aortic valve replacement in 11 patients, after coronary artery bypass with saphenous vein grafts in 4 patients, and after pulmonary valve replacement in 2 patients.

Non-MRSA mediastinitis was caused by *Staphylococcus aureus* sensitive to methicillin in 28 (55%) of 51 patients,

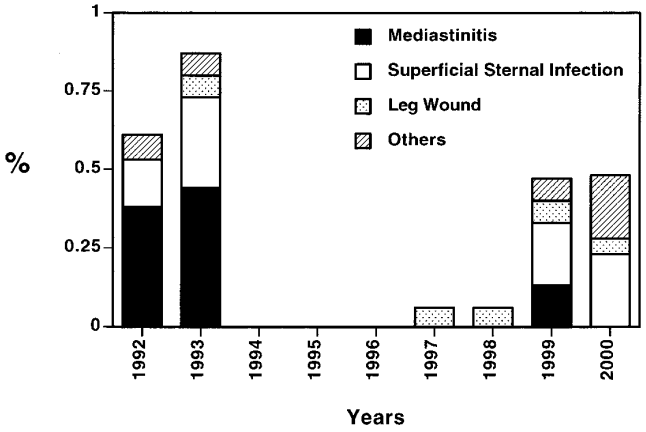

Figure 1. Total incidence of MRSA infections, including mediastinitis, superficial and deep sternal and leg wound infection, and all systemic infection episodes decreased from 1992-1993 to 2000.

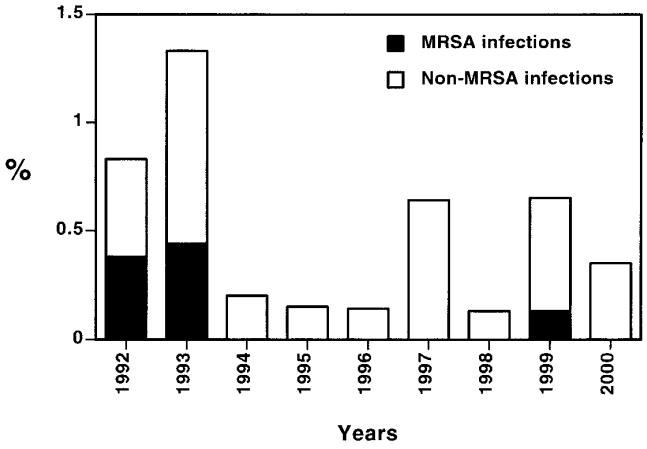

Figure 3. Incidence of MRSA and non-MRSA mediastinal infections decreased from 1992-1993 to 2000.

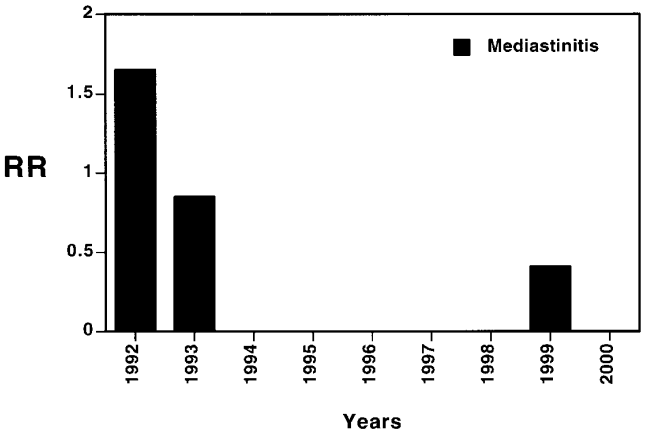

Figure 2. Relative risk *(RR)* of severe mediastinal MRSA infection to all other MRSA infection episodes decreased from 1992-1993 to 2000.

penicillin-sensitive *Staphylococcus epidermidis* in 8 (16%) patients, methicillin-resistant *Staphylococcus epidermidis* in 4 (6%) patients, *Enterobacter cloacae* in 3 (6%) patients, *Enterococcus faecalis* in 2 (4%) patients, and a combination of agents in 6 patients.

Clinical Results

There was 1 (8%) death among 13 patients with MRSA mediastinitis, and 8 (16%) of 51 patients died after non-MRSA acute mediastinitis (P =.7). The causes of death were respiratory and renal failure in the patient with mediastinal MRSA infection and septicemia in 5 patients, mediastinal hemorrhage in 2 patients, and malignant arrhythmia in 1 patient with non-MRSA mediastinal infection.

All patients with MRSA mediastinitis underwent extensive operative mediastinal debridement, with pectoralis muscle flaps in 5 (38%) of 13 and omentoplasty in 2 (15%) of 13 and both reconstructive procedures, pectoralis muscle flaps, and omentoplasty in 1 patient. Nine (18%) of 51 patients with non-MRSA mediastinitis underwent operative debridement with pectoralis muscle flaps and 10 (20%) of 51 patients with omentoplasty (P = .2). The others underwent mediastinal debridement, drainage, and sternal reclosure.

Infection Rates

The first occurrence of MRSA infection in our surgical unit was observed in 1992. The annual incidence of MRSA acute mediastinitis varied from 0.38% (5/1321; 95% CI, 0.12-0.88) of cardiac patients in 1992 and 0.44% (6/1355; 95% CI, 0.16-0.96) in 1993 to 0.13% (2/1528; 95% CI, 0.02-0.47) in 1999 and 0% in 2000. The total incidence of MRSA infection, including mediastinitis, superficial and deep sternal and leg wound infection, and all systemic infection episodes ranged from 0.68% of patients in 1992 and 0.96% of patients in 1993 to 0.46% of patients in 1999 and 0.53% in 2000 (Figure 1). The relative risk of severe mediastinal MRSA infection to all other MRSA infection episodes decreased from 1.65 in 1992 to 0.41 in 1999 (Figure 2).

Although the rate of non-MRSA mediastinal infection did not vary significantly during the study period, the rate of MRSA mediastinitis decreased significantly from 11 infections during the first 2 years of the study (11/2676 [0.41%] patients) compared with only 2 mediastinal infections during the following 6 years (2/11,878 [0.02%] patients, P = .01, Figure 3).

Discussion

The present study shows that MRSA was first isolated in our cardiac surgical unit in 1992 from a patient with acute mediastinitis and was followed by horizontal transmission

to 20 other patients who had various MRSA infections from surgical wound infections to nosocomial bloodstream infections. Horizontal transmission by contiguity is suggested because all MRSA infections occurred with the same biotype in a cluster of patients who underwent surgical intervention during a period of 18 months. Thereafter, 4 preventive measures were initially introduced: nasal screening of all surgical patients, preventive isolation of all carriers, mupirocin ointment applied to the nares of carriers, and vancomycin antibiotic prophylaxis for cardiac surgery of infected patients.[7-10] The preventive measures eradicated MRSA infections from 1994 to 1996, and a low rate of MRSA infection was observed. Then a new rise in prevalence caused by a significant increase in patient referrals from chronically MRSA-contaminated surrounding hospitals was noticed. Nasal screening was at that time extended to all hospitalized patients in an attempt to prevent vertical entry from outside hospital sources and dissemination of MRSA. At the same time, alcohol-based gel for hand washing was introduced to reduce horizontal transmission through staff intermediates because all previous attempts at hand washing reenforcement were not followed by a sustained behavior for more than several weeks.

Thereafter, the incidence of MRSA mediastinitis after cardiac surgery decreased significantly after the implementation of this second set of preventive measures; the incidence of MRSA superficial wound infections and of other MRSA infections remains low. A similar decrease in MRSA infection rates in general hospital settings was reported in Denmark after aggressive preventive measures.[11]

Hospital mortality was low but not significantly different in patients with MRSA compared with those with non-MRSA mediastinitis. MRSA microorganisms are difficult to eradicate from mediastinal tissue, and most MRSA-infected patients needed complex surgical procedures, including pectoralis muscle flaps and omentoplasty.

Several authors have suggested that routine antibiotic prophylaxis for cardiac operations has resulted in a reduction in the incidence of sternal wound infection but resulted also in the emergence of resistant organisms.[3-5] Mossad and colleagues[3] showed not only that *Staphylococcus epidermidis* was responsible for 23% of sternal wound infections in their study but that 92% were caused by methicillin-resistant organisms. In the present study methicillin-sensitive *Staphylococcus aureus* was isolated in 44% of patients, and MRSA was isolated in 20% of patients with mediastinal infections. Thus *Staphylococcus aureus* was the microorganism involved in 64% of mediastinal infection and remains the most important pathogen after cardiac surgery.

The epidemiology of MRSA appears linked to the overuse of antibiotics and, in our experience, is related to referral and transfer of patients already contaminated with the microorganisms from hospitals in which MRSA remains endemic. Although we found no epidemiologic links of any case of MRSA infection, either by surgeon-specific rates, surgical team, or nursing staff, we found a specific association with a donated heart from a subsequently proven MRSA blood culture–positive organ donor, resulting in recipient mediastinal infection after transplantation and postoperative mediastinal MRSA infection in several patients who had been in contact with MRSA carriers in a medical unit of our hospital before surgical intervention. Similar mechanisms of dissemination were also reported by Doebbeling.[12]

Our first set of preventive measures, namely patient screening, preventive isolation, mupirocin ointment in the nares, and vancomycin prophylaxis implemented during the early phase of the study, was effective in eradicating MRSA infections from 1994 to 1996. Because MRSA infections reappeared, albeit at a lower rate, from 1997 to 2000, a new approach in preventive measures, taking more into account "human factors" was applied not only in surgical units but also in all medical units of our hospital to prevent dissemination. Mupirocin in topical application has been used to eradicate nasal colonization with *Staphylococcus aureus* and is also effective against methicillin-resistant *Staphylococcus epidermidis*.[13-15] In Canada screening programs for MRSA have been the recommended guidelines in the Province of Ontario since 1995, with a 90% institutional compliance. Although the incidence of reported MRSA strains is on the rise, it is observed to be mainly through nonnosocomial colonization, resulting in low and stable infection rates.[16]

Jakob and colleagues[17] have not only shown that obesity, diabetes mellitus, and nasal carriage of *Staphylococcus aureus* were independent predictors of sternal wound infection after cardiac surgery but that the endogenous pathway was responsible for the severe wound infections. In their study 28% of patients showed colonization of the nose before the operation, and 16% of these patients had sternal wound infections compared with only 7% of those with normal flora in the nose before surgical intervention. Moreover, 4 of 5 patients with mediastinitis had DNA fingerprints revealing the genotype of *Staphylococcus aureus* isolates from the patient's sternum and nose to be identical. Several authors have also stressed the significance of nasal contamination with *Staphylococcus* pathogens before cardiac surgery.[18-21]

The presence of nasal MRSA colonization of patients before cardiac surgery is especially dramatic because this can lead to direct environmental contamination and dissemination to other patients. Boyce and colleagues[22] showed that 27% of inanimate surfaces sampled in rooms of patients with MRSA were contaminated. Environmental contamination occurred in the rooms of 73% of infected patients and 67% of colonized patients. Sixty-five percent of nurses contaminated their nursing uniforms or gowns with MRSA when they cared for these patients.[22] Thus preventive isolation

appears to be an appropriate measure to prevent dissemination of the resistant microorganism to other patients.

Series of MRSA outbreaks have been reported among surgical patients in intensive care units, in pediatric intensive care units, among chronically instrumented patients, and among patients with previous exposure to antibiotic treatment.[23,24] Although series of MRSA surgical wound infections have not been described in cardiac surgical patients, isolated cases are being reported more often in the literature.[25] Moreover, the routine antibiotic prophylaxis used in cardiac surgery, except for vancomycin, may not protect against MRSA pathogens and can result in surgical wound infection. In our experience MRSA microorganisms minimal inhibitory concentrations showed resistance to a majority of antibiotics, except vancomycin. Given the low prevalence of methicillin and vancomycin resistance among *Staphylococcus aureus* in our population, we chose to restrict vancomycin prophylaxis to contaminated patients or patients allergic to β-lactam and to restrict the therapeutic use to infected patients.[26] Dual or multidrug combinations are also encouraged (eg, vancomycin and a quinolone, vancomycin and rifampin) in hope of preventing resistance.[27,28]

In conclusion, preventive measures, namely nasal screening, preventive isolation, mupirocin ointment, and vancomycin prophylaxis limited to MRSA carriers undergoing cardiac surgery, appear efficacious in controlling MRSA outbreaks and significantly decrease the risk of MRSA mediastinal infection after cardiac surgery. Cardiac patients will remain at risk of severe surgical and systemic infection with highly resistant microorganisms unless all health care providers implement strict measures to prevent the dissemination of multiresistant microorganisms among patients and between hospitals.

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